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This Month in *AJP*

Expression of Myoglobin in Human Cancers

Myoglobin plays important roles in both transporting oxygen and scavenging free radicals in myocytes. Flonta et al (**Am J Pathol: 201–206**) hypothesized that epithelial cancers may also express myoglobin to survive conditions associated with tumor growth such as hypoxia and metabolism of reactive oxygen species. Indeed, human epithelial tumors, including breast, lung, ovary, and colon carcinomas, expressed high levels of myoglobin at early stages of development. In addition, myoglobin was induced in cell lines subjected to hypoxia, oxidative stress, and mitogenic stimulation. Myoglobin expression in carcinomas may therefore protect against the stresses of tumor growth.

Galgt2 Therapy for Muscular Dystrophy

Surrogate gene therapies for muscular dystrophy have limited applicability across different models of dystrophic disease. In disease models with decreased expression of either dystrophin or laminin, overexpression of the glycosyltransferase galgt2, which alters the expression and properties of proteins expressed in skeletal muscle, lessens the symptoms of muscular dystrophy. Xu et al (**Am J Pathol 174:235–247**) examined the effects of galgt2 overexpression in a mouse model of limb girdle muscular dystrophy 2D. Overexpression of galgt2 in α-sarcoglycan-deficient mice resulted in reduced levels of myofiber damage, and adeno-associated virus-mediated postnatal expression of galgt2 protected myofibers from damage. Increasing galgt2 expression may therefore have therapeutic benefits in a broad range of muscular dystrophies.

Endothelin-1 Inhibition in Alzheimer's Disease

Aβ peptide, which accumulates in the brain of Alzheimer's disease patients, is thought to lead to vasoconstriction and reduction of cerebral blood flood. Endothelin converting enzyme-2 (ECE-2) may contribute to cerebrovascular dysfunction by converting the inactive precursor "big endothelin" to the vasoconstrictor endothelin-1. To determine whether ECE-2 plays a role in the vasoconstriction seen in Alzheimer's disease, Palmer et al (**Am J Pathol: 262–270**) examined the neural expression of ECE-2 in patients with Alzheimer's disease and vascular dementia compared with non-demented control patients. ECE-2 levels were elevated in the temporal neocortex of patients with Alzheimer's disease but not vascular dementia. Exposure of a neuroblastoma cell line to Aβ resulted in up-regulation of ECE-2 after 24 hours. These data indicate that ECE-2 levels are up-regulated in response to Aβ and may cause the decrease in cerebral blood flow observed in Alzheimer's disease.

Stromal PDGFβR (Platelet-Derived Growth Factor β Receptor) Expression Correlates with Negative Breast Cancer Prognosis

PDGF α and β receptors are involved in multiple stages of cancer cell growth; however, the contribution of possible stromal expression remains unclear. Paulsson et al (**Am J Pathol: 334–341**) characterized PDGF α and β receptor expression on tumor vessel-associated pericytes and tumor fibroblasts in lymphoma and in colon, ovarian, prostate, lung, and breast cancers. They found that PDGF α and β receptors were independently regulated in the stroma of the tumor types tested, with PDGFβR more frequently expressed on tumor fibroblasts. Colon and prostate tumors expressed the highest stromal levels of PDGFβR. In breast cancer, PDGFβR expression is associated with histological grade, tumor cell proliferation, estrogen receptor expression status, and HER2 status. In addition, stromal PDGFβR expression in premenopausal breast cancer patients significantly correlated with negative prognosis. These data highlight the importance of examining stromal as well as malignant cell expression of PDGF receptors in disease prognosis.

Gastrin and Helicobacter*-Associated Gastric Cancer*

Helicobacter pylori, a major cause of gastric cancer, induces chronic gastritis that leads to atrophy, dysplasia, and finally gastric carcinoma. The mucosal growth factor gastrin is elevated in response to *Helicobacter* infection, and overexpression of gastrin in a mouse model causes gastric cancer. However, gastrin-deficient mice have increased levels of gastric antral tumors. To reconcile this apparent disparity, Takaishi et al (**Am J Pathol: 365–375**) examined the contribution of *Helicobacter* spp infection to gastric cancer in hypergastrinemic, gastrin-deficient, and wild-type mice of similar backgrounds. By 18 months after infection, hypergastrinemic and wild-type mice had severe atrophic gastritis and corpus dysplasia, whereas gastrin-deficient mice had severe gastritis but no corpus dysplasia. However, gastrin-deficient and wild-type mice had antral

dysplasia, whereas hypergastrinemic mice did not exhibit antral pathology. Gastrin, therefore, may have distinct effects between the gastric corpus and antrum and may play a key role in gastric corpus carcinogenesis.

Carbon Monoxide Prevents Arterial Thrombosis

Heme oxygenase-1 (HO-1), which produces iron, biliverdin, and carbon monoxide (CO) during the process of heme degradation, is up-regulated in inflamed or injured tissues and is thought to play a cytoprotective role *in vivo*. Although high levels of CO are toxic, the low levels produced from heme degradation may contribute to the cytoprotective effects of HO-1. To determine whether HO-1 and CO can protect against arterial thrombosis, Chen et al (Am J Pathol: 422–429) examined platelet aggregation in murine aortic allograft recipients. The absence of HO-1 in aortic allograft recipients resulted in significant mortality due to arterial thrombosis. However, treating HO-1-deficient recipients with a CO-releasing molecule significantly reduced platelet aggregation and improved graft recipient survival. Therefore, systemic HO-1/CO plays a key role in protecting against arterial thrombosis in murine aortic allograft recipients.